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CARBENOIDS. METAL ASSISTED IONIZATION[1]

by

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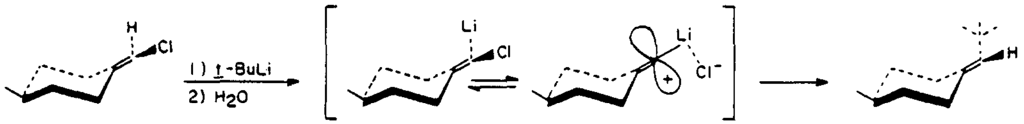
Abstract: Treatment of (S)-(+)-1-chloro-2,2-diphenylcyclopropane with n-butyllithium at -25°C yield, *inter alia*, (R)-(-)-1-*n*-butyl-2, 2-diphenylcyclopropane with *overall inverted* configuration. A metal assisted ionization mechanism is proposed.

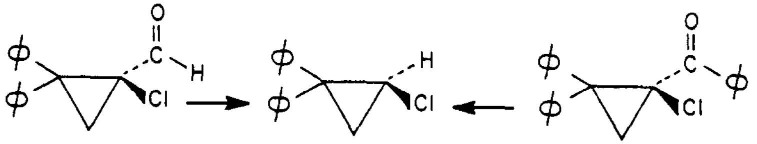
Treatment of vinyl chlorides with an organolithium reagent yields almost exclusively metallation and results in the formation of an alkylidene carbenoid (2)[2,3]. We have recently shown[4] that the carbenoid loses chloride ion *via* a *metal assisted ionization* (MAI) mechanism resulting in the formation of vinyl cation-chloride tight ion-pair[5] (3) which can then be attacked by a nucleophile from the backside. Thus, adding two equivalents of *t*-butyllithium to a tetrahydrofuran solution of chiral (aS)-(+)-4-methylcyclohexylidenechloromethane (1) at -75°C yielded (aR)-(-)-4-methylcyclohexylidene-2',2'-dimethylpropane (4) with *overall inversion of configuration* and an optical purity of 39%. The stereochemistry (racemization with overall inversion) observed in the ionization of 2 to yield 3 is reminiscent of solvolysis reactions involving chiral substrates. Ordinarily vinyl halides ionize with extreme difficulty but carbenoids (metal substituted vinyl halides) appear to ionize more readily (MAI) as evident by the observation[4] that the displacement reaction occurs between temperatures of -75° to -90°C.



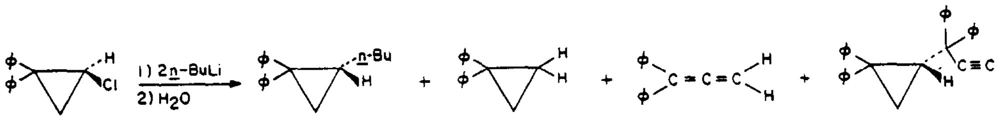
(aS)-(+)-1 2 3 (aR)-(-)-4

In order to further test the concept of MAI another unreactive halide was sought. The system that meets this criterion is the cyclopropyl system since it has been shown that cyclopropyl tosylate solvolyses ~10^6 times slower than cyclohexyl tosylate in acetic acid at 60°C and cyclopropyl chloride solvolyses much slower still[6]. The cyclopropyl system provides us with an additional bonus since if, as we postulated in the vinyl system[4], the carbenoid intermediate can be viewed as a cation then one should observe the usual and facile cyclopropyl to allyl cation rearrangement[6].

The chiral system chosen for this investigation was (S)-(+)-1-chloro-2,2-diphenylcyclopropane (5) which we had prepared previously in connection with other studies[7,8]. It can be prepared either by an Haller-Bauer cleavage of (S)-(+)-1-benzoyl-1-chloro-2,2-diphenylcyclopropane[7] or by the tris(triphenylphosphine)rhodium chloride decarbonylation of (S)-(+)-1-chloro-2,2-diphenylcyclopropanecarboxaldehyde[8]. Both reactions proceed with overall retention of configuration[7,8]. Treatment of (S)-(+)-5 dissolved in tetrahydrofuran with two equivalents of n-butyllithium at -25°C gave a 20% yield of (R)-(-)-1-n-butyl-2,2-diphenylcyclopropane (6) with an optical purity of 51%. Of significance is that the reaction, as in the case of the vinyl halide[4], proceeds with overall inversion of configuration.

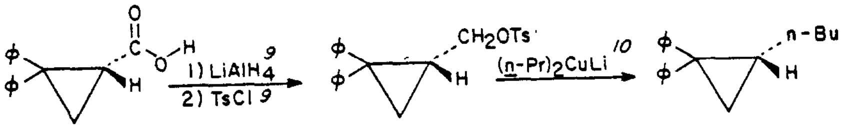


(S)-(+) (S)-(+)-5 (S)-(+)



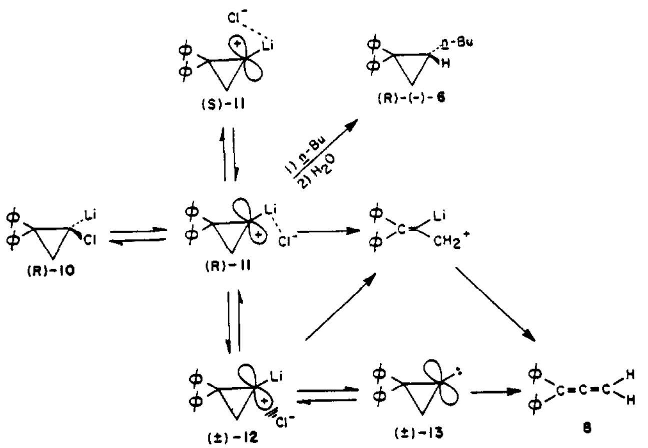
(S)-(+)-5 (R)-(-)-6 7 8 (R)-(-)-9

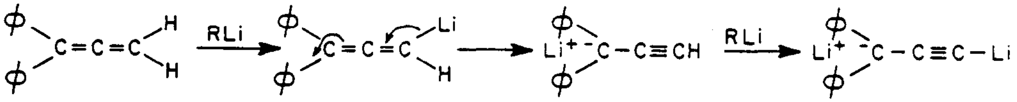
The optical purity and absolute configuration of 6 was determined by converting (R)-(-)-2,2-diphenylcyclopropanecarboxylic acid of known optical purity and configuration[9] to (R)-(-)-6, $[\alpha]^{27}_{Hg}$-193 ± 1° (c, 0.5, $CHCl_3$) by a well established series of reactions that do not involve the chiral center.



(R)-(-) (R)-(-) (R)-(-)

The formation of 7 in 9% yield was not unexpected since a small amount of halogen-metal exchange was anticipated. The products 6,8 and 9 are the result of metallation of 5 to give the carbenoid 10 which undergoes metal assisted ionization to the tight ion-pair 11. Reaction of 11, 12 and 13 with n-butyllithium would account for the formation of R-(-)-6 with overall inversion of configuration but with only 51% optical purity[11]. As expected for cyclopropyl cation intermediates such as 11 and 12, ring opening to an allyl cation would be a major pathway[6,12] which in this case would result in 1,1-diphenylallene (8) formation. The cyclopropylidene carbene 13 can-also ring open to give 8 directly[13]. The yield of 8 however is only 5%. The reason for the apparent low yield is that 8 undergoes further reaction. The acidic allenic protons react with the various organolithium reagents present in the reaction mixture to yield 14. The formation of 14, from the rearrangement of 11, 12 and 13 to 8 followed by the conversion of 8 to 14, accounts for the formation of 9[14], the major product (~50%), in the reaction of n-butyllithium with 5. The formation of 9, $[\alpha]^{25}_{Hg}$-120 ± 1° (c, 0.25, $CHCl_3$) could only have occurred by the reaction of the nucleophile 14 with carbenoids 11 and 12 and carbene 13 as did n-butyllithium. On this basis we have tentatively assigned the R-configuration to 9 which means that overall inversion of configuration has occurred. This result is not dissimilar to that observed in the S_N1 type reactions of chiral halides[15,16].





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1. This work was supported by a grant (CHE-8316493) from the National Science Foundation to whom we are grateful. A NATO Travel Grant (741/84) to one of us (HMW) is also appreciated.

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14. NMR, IR and elemental analysis are consistent with the structure shown for 9. Moreover, X-ray analysis also showed the structure to be assigned. The X-ray analysis will be published elsewhere by Prof. Ivan Bernal, University of Houston.

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16. Other workers notably Nozaki (Kitani, K., Hiyama, T. and Nozaki, H., Bull. Chem. Soc. Jpn. 1977, 50, 1600 and references cited therein) have postulated that inversion at a cyclopropyl carbenoid center occurs by a S_N2 mechanism. Our view is that the carbenoids we have investigated, both cyclopropyl and alkylidene, undergo substitution by an S_N1 type of mechanism[17] and that an S_N2 attack by a nucleophile at a carbenoid carbon is energetically unfavorable.

17. Theoretical studies by P.v.R. Schleyer and K.N. Houk support our conclusions on the alkylidene carbenoid, see, Mareda, J., Rondan, N.G. and Houk, K.N., Clark, T. and Von, P., Schleyer, P.v.R., Clark, T., Kos, A.J., Spitznagel, G.W., Rohde, C., Arad, D., Houk, K.N. and Rondan, N.G., J. Amer. Chem. Soc., 1984, 106, 6467 and references cited therein.

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